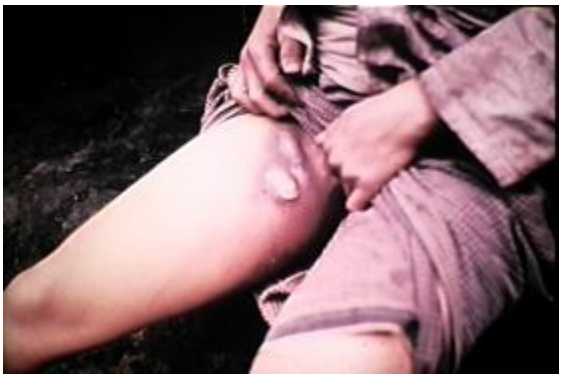
Plague

Disease and Epidemiology

Clinical Description:



Initial signs and symptoms may be nonspecific with fever (which is usually present), chills, malaise (tiredness), myalgia (muscle aches), nausea, prostration, sore throat, and headache.

- If the presentation is "bubonic", then lymph nodes in the inguinal (groin), axillary (armpit), and cervical (neck) areas may become swollen, inflamed, and tender, and may suppurate (discharge pus).
- The presentation may become "septicemic," where the organism becomes disseminated throughout the body including the meninges. Endotoxic shock and disseminated intravascular coagulation (DIC) may occur.
- If the presentation is "pneumonic", pneumonia may be present. Pneumonic plague is especially concerning from an infection control standpoint.
- Plague can also present as "pharyngeal", with an inflamed pharynx, or "meningitis," with nuchal rigidity, or "cutaneous" - but these forms are rare.

Causative Agent:

Plague is caused by a bacterium known as *Yersinia pestis*. Yersinia species are Gram-negative rods that can exhibit a bipolar or "safety pin" staining pattern.

Differential Diagnosis:

Plague can be mistaken for influenza or other acute febrile illnesses.

Laboratory Identification:

If plague is suspected, pre-treatment specimens should be taken if possible, but treatment should not be delayed. The laboratory should be notified if plague is suspected. Plague would be identified as a presumptive isolate at a clinical lab, and then forwarded to a reference lab or to the UPHL for final identification. All hospitals should be encouraged to report even SUSPECT cases of plague, as final identification can be a lengthy process. Specimens should be obtained from appropriate sites for isolating the bacteria, and depend on the clinical presentation. Visualization of bipolar-staining, ovoid, Gram-negative organisms with a "safety pin" appearance permits a rapid presumptive diagnosis of plague.

In cases where live organisms are unculturable (such as postmortem), lymphoid, spleen, lung, and liver tissue or bone marrow samples may yield evidence of plague infection by direct detection methods such as direct fluorescent antibody (DFA) or PCR.

If cultures yield negative results, and plague is still suspected, serologic testing is possible to confirm the diagnosis. One serum specimen should be taken as early in the illness as possible, followed by a convalescent sample 4-6 weeks or more after disease onset.

Treatment:

The drug of choice is streptomycin or gentamicin, however this drug can be difficult to obtain. Tetracyclines, fluoroquinolones and chloramphenicol are also effective. For cases involving meningitis, chloramphenicol is the drug of choice. For optimal efficacy, these drugs should be started within 8-18 hours after disease onset (especially for pneumonic plague). Reappearance of the fever following successful initial therapy may indicate a secondary site of infection. Treatment guidelines and post exposure prophylaxis for possible mass casualty settings can be found in the cited JAMA article in the reference section.

Case Fatality:

The case fatality for untreated bubonic plague is 50-60%. Cases of untreated pneumonic or primary septicemic plague are invariably fatal. Appropriate therapy (if initiated early) will reduce the case fatality rate.

Reservoir:

Plague is a zoonosis involving wild rodents as the natural hosts and their fleas as vectors for the disease. Plague is endemic in rodents throughout the southwestern United States. Ground squirrels are the natural vertebrate host, but it can also be found in rats, prairie dogs, rabbits, hares, wild carnivores, and domestic cats, as well as their fleas.

Transmission:

Typically plague occurs in humans from infected fleas or animals. The organism is transmitted via fleabites, or from bites, scratches, or respiratory droplets, or from handling infected tissues from infected wild or domestic animals. Humans who present with pneumonic plague can spread the disease through respiratory droplets. Humans with bubonic or septicemic plague cannot spread the disease through respiratory droplets, but care must be taken with contact precautions, as the pus from buboes is infectious.

Incubation Period:

The typical incubation period is 1-7 days, and varies with dose and routes of exposure.

Susceptibility:

All people are susceptible to this organism.

Communicability:
Patients with pneumonic plague are considered infectious throughout their symptomatic illness and for 72 hours following initiation of effective antibiotic treatment. Discharge from lesions in patients with bubonic plague is considered infectious.

Epidemiology:
Cases of Plague have occurred sporadically in rural areas of the western United States since the early 1900s. Plague would be considered an endemic zoonotic disease in Utah. In Utah, cats are frequently transmission vehicles. They acquire plague through hunting rodents, develop the disease, and then can transmit the disease.

An average of 7 human cases of plague are reported to the CDC each year in the United States. Utah has about 0.5 cases per year reported through public health. Plague would be considered an endemic zoonotic disease in Utah. In Utah, cats are frequently transmission vehicles. They acquire plague through hunting rodents, develop the disease, and then can transmit the disease.

Public Health Control Measures
Public Health Responsibility:
- Thoroughly investigate all suspect cases of disease
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention
- Initiate active surveillance immediately upon notification of suspect cases

Prevention:
As this disease is a vectorborne illness, public health needs to assure that evidence of endemic activity (either through rodent or flea trapping) is swiftly remediated. Working through sister agencies (such as the Division of Wildlife Resources and the National Park Service) affected rodent burrows should be dusted with pesticides, and warning signs posted to campers/visitors. Information should reinforce not interacting with rodents, etc. Personal protective measures should be used while in a rural area where Plague is endemic; this includes wearing long sleeved shirts and long pants, and tuck pant legs into socks when camping or hiking; use insect repellents containing DEET on exposed skin and clothing. Do not touch squirrels or rodents and stay on hiking trails. Pets should also be kept free of fleas. Large numbers or dead or sick rodents should be reported to the local or state health department.

Vaccine:
No currently licensed vaccine is available.

Chemoprophylaxis:
Detailed treatment guidelines and post exposure prophylaxis for possible mass casualty settings can be found in the cited JAMA article in the reference section.

Prevention in Healthcare Settings:
Contact and droplet precautions are advised for healthcare settings. Patients should be isolated until after 72 hours of appropriate antibiotic therapy. If patients do not have evidence of pneumonic plague, then contact precautions are appropriate.

Outbreaks:
Due to the serious nature of this disease, single cases will be investigated as soon as possible. Public health will assume that a single case could be leading to an outbreak and will react accordingly. Public health will have a large mission of public, clinician, and first responder education in the event of a real outbreak.

Isolation and Quarantine Requirements:
- As this is a disease that is not typically transmitted from person to person, isolation and quarantine are generally not appropriate.
- While the plague bacillus is labile and should not be considered an ongoing threat in an environmental setting. Therefore, no environmental quarantine is necessary.

Case Investigation
Reporting
Plague is an immediately reportable disease in Utah.

Case Definition
Plague (2010)

Clinical Description
Plague is transmitted to humans by fleas or by direct exposure to infected tissues or respiratory droplets; the disease is characterized by fever, chills, headache, malaise, prostration, and leukocytosis that manifests in one or more of the following principal clinical forms:

- Regional lymphadenitis (bubonic plague)
- Septicemia without an evident bubo (septicemic plague)
- Plague pneumonia, resulting from hematogenous spread in bubonic or septicemic cases (secondary pneumonic plague) or inhalation of infectious droplets (primary pneumonic plague)
- Pharyngitis and cervical lymphadenitis resulting from exposure to larger infectious droplets or ingestion of infected tissues (pharyngeal plague)

Laboratory Criteria for Diagnosis
Presumptive

- Elevated serum antibody titer(s) to *Yersinia pestis* fraction 1 (F1) antigen (without documented fourfold or greater change) in a patient with no history of plague vaccination, OR
- Detection of F1 antigen in a clinical specimen by fluorescent assay

Confirmatory

- Isolation of *Y. pestis* from a clinical specimen, OR
- Fourfold or greater change in serum antibody titer to *Y. pestis* F1 antigen

Case Classification

Suspected

A clinically compatible case without presumptive or confirmatory laboratory results

Probable

A clinically compatible case with presumptive laboratory results

Confirmed

A clinically compatible case with confirmatory laboratory results

Comment(s)

The 1996 case definition appearing on this page was re-published in the 2009 CSTE position statement 09-ID-52. Thus, the 1996 and 2010 versions of the case definition are identical.

Classification Tables:

	Case Definition		
Criterion	Confirmed	Probable	Suspected
Clinical Presentation			
fever	C	C	C
chills	C	C	C
headache	C	C	C
prostration	C	C	C
malaise	C	C	C
regional lymphadenitis (bubo)	O	O	O
septicemia	O	O	O
pneumonia	O	O	O
pharyngeal lymphadenitis	O	O	O
healthcare record contains a diagnosis of plague			
death certificate lists plague as a cause of death or a significant condition contributing to death			
Laboratory findings			
leukocytosis	C	C	C

elevated serum antibody titer(s) to *Y, pestis* fraction 1 (F1) antigen (without documented fourfold or greater change) in a patient with no history of plague vaccination		O	
detection of *Y, pestis* F1 antigen in a clinical specimen by fluorescent assay		O	
isolation of *Y. pestis* from a clinical specimen	O		
fourfold or greater change in serum antibody titer to *Y. pestis* F1 antigen	O		
Epidemiological risk factors			
history of exposure to rodents, rodent fleas, wild rabbits, or sick or dead carnivores			
history of being in areas with endemic plague (e.g., NM, AZ, CO, CA, TX)			
work in a microbiology laboratory that handles *Y. pestis* or is in a plague endemic area			
vaccination for plague		A	

Notes:
O = At least one of these "O" criteria in each category (e.g., clinical presentation and laboratory findings)—in conjunction with all other "N" criteria in the same column—is required to classify a case.
A = This criterion must be absent (i.e., NOT present) for the case to meet the reporting criteria or case classification.
C = This finding corroborates (i.e., supports) the diagnosis of—or is associated with—plague, but is not included in the case definition.

Case Investigation Process

Suspect cases of plague should be investigated immediately, even if the cases haven't been confirmed. There are several immediate goals to the investigation process:

- **Notify the UDOH BOE and UPHL and the LHD by phone immediately.**
  - Do not leave a message on an answering machine; you must have a positive contact with an employee at each organization.
- **Actions taken with the case patient**
  - It is important to identify the source of each case. To do this, fill out both the disease investigation form as well as the BT investigation form. The possibility of bioterrorism needs to be ruled out as soon as possible.
  - Identify the type of disease. Is it septicemic, bubonic, or pneumonic?
  - Assure that the infection control precautions are appropriate for the type of disease.
  -

- **Case contact management**
  - Plague is only transmissible from person to person if it is pneumonic.
    - IF the case is pneumonic, then rapid identification of close contacts to the patient from the date of symptom onset until after 72 hours of antibiotic treatment, AND post exposure prophylaxis of those contacts is essential.
  - Pneumonic plague is transmissible via droplets; therefore appropriate contacts should be notified.
  - Assure that contacts receive appropriate prophylaxis.
  - Monitor contacts daily. If any report development of a fever or cough for 7 days after exposure, they should be seen immediately by a clinician.

References

Centers for Disease Control, Case Definitions for Infectious Conditions Under Public Health Surveillance. MMWR 46 (RR-10), 1997.l

Centers for Disease Control and Prevention, National Notifiable Diseases Surveillance System (NNDSS). (June 13, 2012). *Plague (Yesernia pestis).* Retrieved from www.cdc.gov.

Control of Communicable Diseases Manual (19th Edition), Heymann, D.L., Ed; 2008.

Inglesby, et.al., Plague as a Biological Weapon, JAMA 283(17), 2000
Medscape Continuing Education – Terrorism and Disaster: What Clinicians Need to Know: Pneumonic Plague – 2005

Council for State and Territorial Epidemiologists (CSTE) Position statements. Available from URL: http://www.cste.org/default.asp?page=PositionStatements